TITLE
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JOURNAL
Scandinavian Journal of Medicine & Science in Sports

DATE DEPOSITED
19 April 2018

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Article type : Original article

Interface pressure, perceptual and mean arterial pressure responses to different blood flow restriction systems.

Running title: Pressure in blood flow restriction systems

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As the corresponding author, I can confirm that this manuscript has been read and approved by all the listed co-authors. The manuscript contains original material that has not been previously published and is not currently under consideration elsewhere until a final decision by the editorial board as to its suitability for this journal has been made.

Abstract word count: 249
Number of tables and figures: 5

Abstract

This study examined the cuff to limb interface pressure during blood flow restriction (BFR), and the perceptual and mean arterial pressure responses, in different BFR systems. Eighteen participants attended three experimental sessions in a randomised, crossover, counterbalanced design. Participants underwent inflations at 40% and 80% limb occlusive pressure (LOP) at rest and completed 4 sets of unilateral leg press exercise at 30% of one repetition maximum with BFR at 80% LOP. Different BFR systems were used each session: an automatic rapid-inflation (RI), automatic personalised tourniquet (PT) and manual handheld pump and sphygmomanometer (HS) system. Interface pressure was measured using a universal interface device with pressure sensors. Perceived exertion and pain were measured after each set, mean arterial pressure (MAP) was measured pre-, 1-min post- and 5-min post-exercise. Interface pressure was lower than the set pressure in all BFR systems at rest ($p<0.05$). Interface pressure was, on average, 10 ± 8 and 48 ± 36 mmHg higher than the set pressure in the RI and HS system ($p<0.01$), with no differences observed in the PT system ($p>0.05$), during exercise. Pain and exertion were greater in sets 3 and 4 in the RI and HS system compared to the PT system ($p<0.05$). MAP was higher in the RI and HS system compared to the PT system at 1-min and 5 min post-exercise ($p<0.05$). BFR systems applying higher pressures amplify mean arterial pressure and perceptual responses. Automatic BFR systems appear to regulate pressure effectively within an acceptable range during BFR exercise.

Key words: occlusion, pressure control, tourniquet pressure, effectiveness

Introduction

The technique of blood flow restriction (BFR) applied both passively and in combination with exercise has become a world-wide research interest. Passive application of BFR may attenuate decreases in limb circumference [1] and strength loss [2] during periods of unloading. Combining BFR with light load resistance training can improve muscle strength in load-compromised individuals without the traditionally required heavy loading of a limb [3], leading to suggestions of its use as a clinical rehabilitation tool [3,4]. Different cuff types and sizes influence perceptual [5] and cardiovascular (CV) [6] responses to BFR exercise, thus BFR is commonly applied as a relative percentage of total arterial limb occlusive pressure (LOP) to standardise occlusion across cuffs and cohorts [7]. The cuffs used to achieve BFR in this manner are typically part of a pneumatic BFR system, which also includes a device used for inflation of the cuff. Within the literature, a variety of BFR systems are used, including automatic rapid-inflation, manual handheld sphygmomanometer and automatic personalised tourniquet systems.

However, several aspects of these BFR systems are unknown. The actual pressure between the cuff and the limb during application of BFR in the different BFR systems is unclear and has not been systematically examined to date. It is conceivable that if differences between the set pressure on the system and the cuff-to-limb interface pressure exist and vary between different BFR systems, this may influence perceptual and CV responses to exercise. The distribution of pressure under a tourniquet can result in structural damage to underlying nerves and tissues if exposed to higher shear forces from mechanical compression for prolonged periods of time [8,9]. Although BFR exercise is typically of short duration (~5-10 minutes) and thus the risk is likely small (particularly when BFR is individualised to LOP), the risk may be exacerbated during rare reports of prolonged continuous passive BFR application (>30 mins) [10]. Though the safety of BFR training has been reviewed [3], any changes in interface pressure during BFR both passively and concomitantly with exercise may contribute to the risk of subcutaneous tissue injury. It is therefore important to examine the interface pressure during BFR in different BFR systems commonly used, and the influence on physiological responses. Thus, the overall objective of this study was to examine the cuff to limb interface pressure during passive BFR and BFR exercise, and the perceptual and mean arterial pressure (MAP) responses, in different pneumatic BFR systems.

Materials and methods

Participants

Eighteen male participants (Mean ± standard deviation: age = 27 ± 5 y; body mass = 88.5 ± 25.9 kg; height = 174.86 ± 23.29 cm; body mass index = 28.94 ± 3.28 kg.m^2; blood pressure = 129 ± 9/77 ± 9 mmHg) volunteered to participate. Participants were recreationally active, all had performed resistance exercise previously and were currently averaging 3 days/week. All were active, non-smokers, free from cardiovascular, pulmonary and metabolic diseases and musculoskeletal injuries in the past 12 months. Participants refrained from strenuous exercise, caffeine and alcohol in the 24 h prior to testing sessions,

and maintained normal dietary habits for the study duration. All participants provided signed informed consent, in compliance with the Declaration of Helsinki, 7th version, October 2013 [11]. All protocols were approved by the University ethical committee.

Experimental protocol

Participants first attended a familiarisation session, including a medical health screening. This was followed by three testing sessions in a randomised crossover counterbalanced design, each including a rest and exercise trial. All sessions were separated by a minimum of 48 h. In the familiarisation, height and body mass were recorded to the nearest 0.01 cm and 0.1 kg, respectively; blood pressure was measured in a supine position at the brachial artery; unilateral concentric one repetition maximum (1RM) of the dominant leg was tested according to previous procedures [12] and participants were familiarised to the BFR protocols.

The same experimental protocol was implemented for all three testing sessions, using a different BFR system and its respective cuff each time: an automatic rapid-inflation (RI) system (E20 rapid cuff inflator, Hokanson, Bellevue, WA, USA) with a straight nylon RI cuff (13 cm x 124 cm, 0.5 mm thick); an automatic personalised tourniquet (PT) system (Delfi Medical, Vancouver, BC, Canada) with a variable contour nylon cuff (11.5 cm x 86 cm, 2.5 mm thick); a manual handheld (HS) pump and sphygmomanometer system with straight nylon cuff (8 cm x 100 cm, 1.5 mm thick) (Occlusion Cuff, Sussex, London, UK). Each BFR system comprises a method of pressure regulation: the RI system adjusts pressure automatically; the PT system automatically adjusts pressure around the set pressure [13]; and the manual HS system does not automatically regulate pressure. Cuff thickness was measured manually with the cuff unraveled; as it was not possible to measure the thickness of the layer of cuff material that would be in contact with the skin without damaging the cuffs, thus our measures likely accounted for double the thickness of the actual layer in contact with the skin, we halved our measures to more appropriately represent this layer. Tubing lines were inserted into the bladders of all cuffs and sealed with airtight UV bonds to allow pressure within the cuff bladders to be measured. In a supine position, the cuff was placed on the proximal portion of the upper dominant leg. Limb circumference was measured at the midpoint of each cuff then divided by 4 to provide the positions for taping pressure sensors medially, anteriorly, laterally and posteriorly, to examine all tissue areas compressed by the cuff [14] at the midpoint where perineural pressures peak [15]. Preliminary pilot work determined individual sensors provided a reliable and valid measure of interface pressure. The cuff was replaced on the leg, the cuff bladder port was connected to the sensor device, and LOP was calculated using Doppler ultrasound at the posterior tibial artery according to previous procedures [16] (Figure 1). For the rest trial, lying supine on a treatment bed participants underwent 2 x 1 min inflations at 40% and 80% LOP, in that order, separated by 5 min of rest [17,18]. Participants then moved to the leg press, resting for 10 min before beginning the exercise trial. The exercise experimental protocols involved unilateral leg press

exercise and were matched for load (30% 1RM), sets (4), repetitions (75), pressure (80% LOP) and contraction cycle (1 s concentric/1 s eccentric) using a metronome. No manual adjustments to pressure were made on any BFR system during any trials.

Perceptual and mean arterial pressure response

Ratings of perceived exertion (RPE) (6-20)[19] and pain (0-10)[19] were measured following each set. Participants received verbal instructions on rating both during the familiarisation visit and were reminded on each subsequent visit. For pain, participants were informed that 10 was their reference point which represented their previous worst felt pain, and that they could give a score of 11 if the pain was worse than any they had ever felt before, which is similar to previous research examining discomfort during BFR [20,21]. For RPE, it was explained to participants that a rating of 6 meant they felt no exertion, and 20 meant they were giving maximal effort and could not exert themselves any further [21]. MAP was measured pre-, 1-min post- and 5-min post-exercise using a Mobil-O-Graph ambulatory blood pressure monitor connected to Hypertension Management Software (IEM, Cockerillstrasse, Stolberg, Germany) on a laptop. This monitor measures peripheral (brachial) blood pressure and collects the heart beat (rate), systolic and diastolic data from the individual, recording the peripheral pulse wave. The Hypertension Management software utilizes a general transfer function to derive an ascending aortic pulse wave, which is used alongside the various measurements to calculate a range of central arterial indices, including MAP.

Measurement of interface pressure

The pressure measurement system comprised a wireless digital connection system, a universal interface device and Pasco Capstone software (Sparklink, Pasco Scientific, Roseville, CA, USA). Interface pressure during BFR was measured using the interface device, connected to two Pasco quad pressure sensors. One sensor had four flexible circular pillow pads attached (Microlab Elettronica, Ponte S. Nicolo, PD, Italy); the other sensor had a channel to connect to a tube line from the cuff bladder, which was inserted into the bladder of each cuff and sealed with an airtight UV bond. Each pad has a 2 cm diameter, connected to the sensor with 50 cm of hard, non-compressible tubing 3 mm in diameter. A four-way giving tap was connected 5 cm from each tube attachment to the quad sensor to allow introduction and removal of air into and out of the pillow pads by an empty 50 ml giving syringe. Prior to application the pad and tubing were completely deflated, 10 ml of air was introduced and then the four-way tap was closed, and the syringe removed; this was repeated for all channels. The interface device was connected to Capstone data collection software (Capstone Version 3.2.1, Pasco, Roseville, CA, USA) which sampled sensor signals continuously at a rate of 20 Hz to produce a pressure trace. Prior to each trial sensors were calibrated to 0 mmHg following application of the cuff to the leg, to control for any possible confounding effect of initial pressure due to securing of the cuff around the limb. Mean ± SD (mmHg) for BFR inflation periods were calculated for the middle 30 s of each 1 min

inflation at REST, to account for cuff inflation time to the set pressure and to restrict measurement to the period in which full inflation was maintained [14]. Pressure was measured continuously during exercise; the Capstone software calculated the mean ± SD for interface pressure from the beginning of the first repetition to the end of the final repetition for each set of exercise.

Statistical analyses

Pressure data was analysed using the R package (V3.4.0). The Bland and Altman method [22] was used to examine differences between the set pressure and the interface pressure for the 2 x rest trials and the 4 sets in the exercise trial for each BFR system. Limits of agreement (LOA) were established to assess the relative bias (mean difference) and random error (1.96 SD of the difference) between the set pressure and interface pressure with 95% confidence intervals (CI). A clinical limit of ± 15 mmHg was set *a priori*, as this is the recommended maximum/minimum pressure window for a surgical tourniquet designed to safely and effectively restrict blood flow [23]. A paired sample t-test investigated differences between the set pressure and interface pressure. Analysis of MAP and perceptual responses was performed with IBM SPSS Statistics Version 22.0 using two-way (cuff x time) repeated measures ANOVAs. For any statistically significant two-way interaction, paired sample t-tests with Bonferroni correction were used for post-hoc analysis to determine individual differences. Alpha significance was set *a priori* $p<0.05$.

Results

All 18 participants completed the study with no adverse events. All 75-repetitions were completed in all participants across all exercise trials. No order effect was noted for ratings of perceived pain and exertion. Mean ± SD for BFR pressures, load, leg circumference and sensor placement are detailed in Table 1. Data were normally distributed for all trials across all three BFR systems ($p>0.05$).

Interface pressure

Rest

For the RI system, interface pressure was 5 ± 5 mmHg lower than the set pressure (95% CI, -13.84-4.50, $p<0.05$) at 40% LOP, and 5 ± 5 mmHg lower than the set pressure (95% CI, -15.19-5.41, $p<0.05$) at 80% LOP (Figure 2, A & B, respectively). For the PT system, interface pressure was 8 ± 4 mmHg lower than the set pressure (95% CI, -16.84 to -0.17, $p<0.05$) at 40% LOP, and 9 ± 4 mmHg lower than the set pressure (95% CI, -16.80 to -0.32, $p<0.05$) at 80% LOP (Figure 2, C and D, respectively). For the HS system, interface pressure was 20 ± 10 mmHg lower than the set pressure (95% CI, -39.16 to -1.40, $p<0.05$) at 40% LOP, and 37 ± 13 mmHg lower than the set pressure (95% CI, -62.12 to -11.88, $p<0.05$) at 80% LOP (Figure 2, E and F, respectively). Mean differences between set pressure and interface pressure were within the ± 15 mmHg limit for both the RI and PT systems.

Exercise

For the RI system, compared to the set pressure the interface pressure was 11 ± 7 mmHg higher (95% CI, -2.80-24.91, p<0.01), 10 ± 8 mmHg higher (95% CI, -5.77-25.66, p<0.01), 10 ± 8 mmHg higher (95% CI, -6.66-26.44, p<0.01), and 10 ± 9 mmHg higher (95% CI, -6.61-26.72, p<0.01) for sets 1, 2, 3 and 4, respectively (Figure 3, G, H, I and J, respectively). Mean differences between set pressure and interface pressure was statistically significant across all sets (p<0.01) and were within the limit of ± 15 mmHg. For the PT system trial, there were no significant differences between the set pressure and interface pressure during all exercise sets (Figure 3, K, L, M, N for set 1, 2, 3 and 4, respectively, all p>0.05). Pressure differences were within the limit of ± 15 mmHg. For the HS system, compared to the set pressure the interface pressure was 62 ± 35 mmHg higher (95% CI, -6.79-130.57, p<0.01), 47 ± 38 mmHg higher (95% CI, -27.52-121.96, p<0.01), 44 ± 34 mmHg higher (95% CI, -23.11-111.89, p<0.01), and 37 ± 36 mmHg higher (95% CI, -33.79-108.01, p<0.01) for sets 1, 2, 3 and 4, respectively (Figure 3, O, P, Q and R, respectively). All differences between set pressure and interface pressure were statistically significant across all sets (p<0.01) and exceeded the limit of ± 15 mmHg.

Pain

There was a statistically significant two-way interaction between the type of BFR system and time ($F_{(3.05, 51.80)} = 6.72$, p<0.01). There was a tendency for pain to be higher in the HS system compared to the PT system trial after set 1 (3.0 ± 1.6 vs 2.0 ± 1.4, respectively, 95% CI 0.202 to 1.731, p=0.01) (Table 2). There was no significant difference in mean pain scores after set 2 of exercise (p=0.07) (Table 2). After set 3, pain was higher in the RI system compared to the PT system (6.3 ± 2.8 vs 4.8 ± 1.8, 95% CI, 0.449 to 2.551, p<0.01), and higher in the HS system compared to the PT system (7.0 ± 2.5 vs 4.8 ± 1.8, 95% CI, 0.887 to 3.558, p<0.01) (Table 2). After set 4, pain was higher in the RI system compared to the PT system (7.9 ± 2.3 vs 5.7 ± 2.0, 95% CI, 0.212 to 3.171, p<0.01), and higher in the HS system compared to the PT system (8.3 ± 2.3 vs 5.7 ± 2.0, 95% CI, 1.359 to 3.808, p<0.01) (Table 2).

RPE

There was a statistically significant two-way interaction between the type of BFR system and time ($F_{(3.15, 53.50)} = 30.53$, p=0.03). There were no significant differences in RPE after set 1 of exercise (p>0.01). RPE was higher in the HS system compared to the PT system after set 2 (14 ± 1 vs. 13 ± 0, 95% CI, 0.517 to 2.705, p<0.01) (Table 2). RPE was higher in the HS system compared to the PT system after set 3 (16 ± 2 vs. 14 ± 2, 95% CI, 0.234-2.988, p=0.02) (Table 2). RPE was higher in the HS system compared to the PT system trial after set 4 (17 ± 2 vs 15 ± 2, 95% CI, 0.794 to 3.095, p<0.01) (Table 2). RPE was higher in the RI system compared to the PT system after set 4 (17 ± 2 vs. 15 ± 2, 95% CI, 0.725 to 2.053, p<0.01) (Table 2).

Mean arterial pressure

There was a statistically significant two-way interaction between the type of BFR system and time ($F_{(4, 68)} = 4.30$, $p<0.01$). MAP was not statistically significantly different between the BFR systems at the pre-exercise time point ($p>0.01$) (Table 2). At 1-min post-exercise, MAP was significantly higher in the RI system compared to the PT system, a mean difference of 10 ± 6 mmHg (95% CI, 5.030 to 15.748, $p<0.01$), and significantly higher in the HS system compared to the PT system, a mean difference of 11 ± 6 mmHg (95% CI, 5.558 to 16.190, $p<0.01$) (Table 2). At 5-min post-exercise, MAP was significantly higher in the RI system compared to the PT system, a mean difference of 9 ± 7 mmHg (95% CI, 2.701 to 14.410, $p<0.01$), and significantly higher in the HS system compared to the PT system, a mean difference of 11 ± 5 mmHg (95% CI, 5.854 to 15.813, $p<0.01$) (Table 2). At 5-min post-exercise, MAP was higher compared to pre-exercise in the HS system, a mean difference of 6 ± 8 mmHg (95% CI, 2.166 to 10.056, $p<0.01$), and lower compared to 1-min post-exercise in the PT system, a mean difference of -6 ± 7 mmHg (95% CI, -9.325 to -2.675, $p<0.01$) (Table 2).

Discussion

The present study was, to the author's knowledge, the first in-vivo study of the interface pressure during BFR exercise across different BFR systems. The main findings were: 1) interface pressure was lower than the set pressure at both 40% and 80% LOP in all three systems during passive BFR; 2) interface pressure was higher than the set pressure in both the RI system and HS system exercise trials, exceeding the limit of ± 15 mmHg in the HS system, with no significant differences observed in the PT system; 3) Higher perceptual responses were observed in the RI system and HS exercise trials compared to the PT system; and 4) A greater post-exercise MAP response was observed in the RI system and HS system exercise trials compared to the PT system.

The passive application of BFR in early post-surgical contexts before ambulation may maintain muscle strength [2]. In the present study, there was a global drop in interface pressure compared to set pressure during passive BFR in all three BFR systems; the pressure difference was within the clinical limit of ± 15 mmHg in only the RI system and PT systems. Ex-vivo studies have demonstrated that pressure decreases as depth within the compressed tissues increases [24], however the present study demonstrates a pressure difference is already apparent during transference from cuff to limb. This was evidenced in a study that measured cuff-limb interface pressure in tourniquets applied during surgery [14]. Comparison of the set pressure and cuff bladder pressure in the present study indicated small differences in all three BFR systems, suggesting that pressure is likely not lost during transference from the inflation device to the inside of the cuff. A more compelling explanation is that pressure is lost during transference from cuff to limb, perhaps due to cuff material and thickness. Cuffs composed of more durable material, such as the thicker (2.5 mm) nylon cuff in the PT system, likely provide greater cushioning, and each layer of cushioning may divert a portion of the exerted pressure which therefore is no longer passed onto the underlying limb [14]. This would support the findings of the present study, as the straight nylon RI cuff

was the thinner than the variable contour cuff in the PT system and straight nylon cuff in HS system (0.5mm vs 2.5 mm vs 1.5 mm, respectively) and provided the smallest deviation from the set pressure during passive BFR. However, the method of pressure control within the BFR system (i.e automatic or manual) may also have an influence on the deviation from the set pressure, with the systems designed to automatically adjust pressure likely contributing to smaller deviations from the set pressure. Additionally, cuff material may reduce pressure maintenance within the cuff itself, which may partially explain the substantial loss of pressure in the straight nylon cuff within the HS system. The shape of the cuff may also contribute to the observed drop in pressure; contoured cuffs that lie more snugly around the limb may attenuate pressure loss given the greater circumferential proximity with the limb. At present this is speculative and the influence of specific cuff materials, shape and thickness on cuff-to-limb pressure transference during BFR has not been systematically examined. Additionally, other factors such as limb position, composition and contractile state may have an influence. However, what is known from the present study is that the RI nylon cuff was the thinnest (0.5 mm) and the nylon variable-contour cuff was contoured, with both applying pressure more effectively compared to the straight nylon cuff within the HS system. Although speculative at present, the greater thickness of the HS system cuff compared to the RI system cuff (1.5 mm vs 0.5 mm), and the straight vs contoured fit compared to the nylon cuff within the PT system, may have had a synergistic effect contributing to the greater loss of interface pressure. Thus, a thinner or contoured cuff may be best for use in passive BFR application.

During exercise the interface pressure was significantly higher than the set pressure in both the RI and HS systems across all sets of exercise. No significant differences were found between the set pressure and interface pressure in the PT system, again across all sets of exercise. However, based on the results of the present study, pressure appears to exceed the clinically acceptable limit in the HS system only. The results of the present study suggest that the RI and HS systems may be applying higher pressures; however, the set pressures on the device and cuff bladder pressures were similar. Thus, a more feasible explanation is that the increase in interface pressure is due to a synergistic combination of concentric muscle action against the inflated cuff and the BFR systems method of pressure control. Given the dynamic nature of BFR exercise, it is deducible that there will be fluctuations in interface pressure with concentric and eccentric muscle action. In BFR systems that are not designed to automatically adjust pressure by deflating during the concentric phase of contraction, such as the HS system, an increase in interface pressure would be observed. The PT system is designed to automatically regulate pressure by deflating during the concentric phase of contraction, which would explain the observation of no difference between the set pressure and interface pressure during exercise. Although the RI system similarly adjusts pressure in this manner, it is possible that the deflation response to underlying concentric muscle contraction is not as rapid as that of the PT system. Higher pressures may result in complete arterial occlusion; it has been hypothesised that this may increase the risk of an adverse event

[21], and excessive and prolonged pressures risk damage to structures beneath the cuff [8]. Therefore, it seems a sensible and desirable conclusion that a BFR system can adjust pressure in response to any increase in interface pressure that may be caused by muscle contraction against the system's cuff, as this may help minimise any risk of tourniquet-induced injury. Although our findings are specific to the BFR systems included in the present study, which itself is not without its limitations, they suggest that interface pressure may be different to the set pressure in other BFR systems with different methods of pressure control used within the literature.

When implementing tourniquet occlusion clinically, patients should be monitored continuously for pain and hypertension [8] which may dictate work volume and patient adherence [25]. In the present study, pain was significantly higher in the RI and HS systems compared to the PT system in sets 3 and 4, when cuffs were set at the same relative pressure of 80% LOP. The RI and HS systems were found to elicit pressures that were 9-11 mmHg and 37-62 mmHg higher than the set pressure, respectively, which may contribute to the exacerbated pain response in the load and repetition matched conditions. Research has shown increases in discomfort with higher pressures [20,26]. Higher BFR pressures may cause greater metabolite accumulation [27]; it has been suggested that the resultant acidic intramuscular environment can increase sympathetic nervous system activity, partially mediated by group III and IV afferent fibres [28]. Jessee et al. (2017) recently suggested that higher pressures and stimulation of these group afferents in this manner may increase perception of discomfort. Wider cuffs were less painful than narrow cuffs when set at relative pressures in a crossover study [29], likely owing to the fact that they provide better transmission of tissue compression [30] and require less pressure to effectively occlude blood flow [20]. This may explain why the straight nylon cuff in the HS system, which was the narrowest at 8 cm width and had the highest LOP, produced the highest pain. In contrast, Rossow et al. (2012) reported that wide cuffs caused greater pain responses compared to narrow cuffs when set at a relative pressure of 130% brachial systolic blood pressure. It is possible that a combination of the method of pressure control in the BFR system and the properties of the two different cuffs may explain the findings of this study. In the present study, the RI cuff was wider (13 cm) and had a lower LOP compared to the narrower PT cuff (11.5 cm) yet caused significantly more pain during sets 3 and 4 of exercise. The higher interface pressures observed in the RI system may partially explain the increased pain. Additionally, Buckner et al. (2017) examined the acute perceptual response to upper limb BFR exercise in narrow elastic and nylon cuffs of similar width (3 cm vs. 5 cm, respectively), observing greater discomfort in sets 2, 3 and 4 in the elastic cuff despite both cuffs set at a relative pressure. The authors suggested that higher pressures applied by the elastic cuff and differences in the material and pliability of cuff type throughout the range of motion may contribute to exacerbated perception of pain. These findings are contrary to that of Loenneke and colleagues, who reported no differences in acute perceptual responses to lower limb BFR exercise between nylon and elastic cuffs [31]. This may be due in part to anatomical limb differences or the use of pressures based on thigh circumference, as opposed to relative to LOP, in the

lower-limb study. Finally, although cuffs of different material but similar width require similar arterial occlusion pressures [32], contoured cuffs may fit the limb better. This may increase comfort and evenly distribute pressure, which may contribute to reduced pain observed in the PT system. It is of note that the pain scores observed in the present study appear higher compared to previous studies. This may be due to selection of a high pressure (80% LOP) and the volume of exercise: in previous research participants typically do not complete all reps in the later BFR sets. In the present study, the participants completed all reps in the later sets and thus spent more time under BFR, which may contribute to higher perceptions of pain alongside a high set pressure and also the changes in interface pressure during exercise, caused in part by the method of pressure control. However, more research is required to further understand the interactions between factors such as cuff properties, participants factors and BFR controlling system factors.

Increases in perceived exertion are typically associated with increased load [33]. RPE during BFR exercise is reported to be similar across relative pressures at matched loads [5]. The present study found differences in RPE between the cuffs during sets 1, 3 and 4, despite matched loads and volume. Research reports that RPE is amplified by increasing pressure and load [20], evidenced by rises in RPE, alongside increases in discomfort, as pressure increased from 10-90% LOP during load-matched upper body exercise at 30% 1RM [26]. Although the present study set relative pressures of 80% LOP for all three BFR systems, analysis of interface pressure revealed that pressures applied to the limb in the RI and HS systems were higher than the set pressure; these cuffs also produced higher pain scores compared to the PT system. It has been proposed that ischemic pain and decreased metabolite clearance, potentially caused by higher pressures and greater mechanical compression in the present study, may create a heightened perception of discomfort and exertion [34]. This signifies a possible synergistic effect of pressure and mechanical compression on both perceived exertion and pain. It should be acknowledged that these ratings are not particularly high, and that perceptual responses to light load (30% 1RM) BFR exercise are lower compared to an equivalent form of exercise at heavier loads (70%1RM) [34]. Together with demonstration of a similar time course of adaptation to perceptual responses between light load BFR and heavy load exercise [25], this supports the feasibility of BFR as a clinical rehabilitation tool.

Higher BFR pressures may evoke greater CV responses [35]. Efforts to reduce concerns of amplified CV responses suggest that relative pressures be used [20,21]. The present study demonstrated greater post-exercise MAP responses in the RI and HS systems, with both remaining elevated at 5-min post-exercise compared to the PT system, when all BFR systems were set at a relative pressure of 80% LOP. As previously stated, 80% LOP was higher in the PT system compared to the RI system, yet it produced a smaller post-exercise MAP response that had returned to baseline by 5 min post-exercise. Recent research demonstrated similar levels of blood flow reduction at rest between different cuffs when set at relative pressures between 40-90% LOP [36]. Although speculative at present, the dynamic nature of BFR

exercise and associated increase in interface pressure in certain BFR systems may contribute to greater mechanical compression, which could possibly influence limb blood flow at relative pressures in different BFR systems and contribute to an augmented MAP response. It is of note that CV responses are similar during light load BFR training to heavy load training [37]. Additionally, peak CV response to unilateral BFR exercise is likely lower than observed in bilateral exercise with greater muscle mass involvement [38]. The MAP responses to different BFR systems may only provide cause for concern if higher applied pressures place an individual under complete arterial occlusion, or when BFR is applied in patients who are hypertensive [39] or have heart disease [40], where augmentation of exercise-induced heart rate increases have been observed.

The present study is not without limitations. The pressure sensors used have their own associated error (± 1 mmHg), therefore the results of pressure changes within each BFR system are likely specific and relative to the pressure sensor system used. Additionally, our method of deriving an average of the interface pressure across all sets in the entire exercise bouts does not allow for us to examine specifically the magnitude of increases with concentric contraction and decreases with eccentric contraction, and the respective influence of each in the calculation of the mean pressure. Future research is needed to determine the magnitude of pressure change throughout different muscle contractile phases. The differing cuff properties in each BFR system may influence control of pressure by the inflation device; as these were not compared directly, discussion of the potential influence is speculative at present. We could not quantify leg blood flow during BFR exercise, thus our suggestions on how interface pressure changes during dynamic exercise may influence vasculature compression are hypothetical. Although we believe a maximum pressure limit is necessary for safe BFR application, we acknowledge the ± 15 mmHg regulation limit discussed in the present study may be small for the variation likely observed during exercise. Finally, our results may be specific to the male population as no females were included in the present study, and factors such as subcutaneous tissue composition and the menstrual cycle may affect aspects such as blood pressure and pressure control during BFR. Although correlational analysis indicated no relationship between BMI and the pressure difference in the present study, investigation of the influence of BMI on pressure control within BFR systems may have important implications for BFR prescription.

To conclude, interface pressure appears to be different in different BFR systems when applied passively, likely owing to cuff material, thickness and shape, and other potential factors relating to the participant and the pressure control system within each BFR system. Higher interface pressure during exercise may be attributed to a combination of muscle contraction, method of pressure control, cuff properties and participant factors. A BFR system that automatically adjusts pressure during exercise and causes reduced perceptual and MAP responses is likely the most beneficial clinical tool that may positively influence patient tolerance and adherence to a BFR rehabilitation programme.

Perspectives

Interface pressure between the cuff and the limb in different BFR systems, and the influence on perceptual and MAP responses, has not been examined to date. It is important to examine interface pressure during passive BFR and dynamic BFR exercise as excessive pressures may increase the risk of tourniquet-induced injury [8,9], and may also influence perceptual and MAP responses to BFR exercise which in turn may influence exercise tolerance and adherence to a clinical BFR rehabilitation programme [25]. In this study, we examined the interface pressure during passive BFR and BFR exercise in three different BFR systems commonly used in the literature. Interface pressure appears to be lower than the set pressure in all systems when BFR is applied passively, which we hypothesize may be a result of pressure control and cuff properties within the BFR systems. Additionally, it appears that interface pressure can be higher than the set pressure during BFR exercise, likely due to the method of pressure control, cuff properties and contraction cycle, which appears to influence the perceptual and MAP response to BFR exercise.

Acknowledgments

This study was supported by Delfi Medical Innovations Inc. who provided a pneumatic variable contour cuff and PT system device for the study, and inserted UV bond sealed lines into the bladders of all cuffs to allow us to measure pressure inside the cuff bladders.

Conflicts of interest

The authors declare no conflicts of interest

References

1. Kubota A, Sakuraba K, Sawaki K, Sumide T, Tamura Y. Prevention of disuse muscular weakness by restriction of blood flow. *Med Sci Sports Exerc*. 2008;40(3):529-534. doi:10.1249/MSS.0b013e31815ddac6.
2. Kubota A, Sakuraba K, Koh S, Ogura Y, Tamura Y. Blood flow restriction by low compressive force prevents disuse muscular weakness. *J Sci Med Sport*. 2011;14(2):95-99. doi:10.1016/j.jsams.2010.08.007.
3. Hughes L, Paton B, Rosenblatt B, Gissane C, Patterson SD. Blood flow restriction training in clinical musculoskeletal rehabilitation: A systematic review and meta-analysis. *Br J Sports Med*. 2017;51(13):1003-1011. doi:10.1136/bjsports-2016-097071.
4. Patterson SD, Hughes L, Head P, Warmington S, Brandner C. Blood flow restriction training: A novel approach to augment clinical rehabilitation: How to do it. *Br J Sports Med*. 2017;51(23):1648-1649. doi:10.1136/bjsports-2017-097738.
5. Loenneke JP, Kim D, Mouser JG, et al. Are there perceptual differences to varying levels of blood flow restriction? *Physiol Behav*. 2016;157:277-280. doi:10.1016/j.physbeh.2016.02.022.
6. Brandner CR, Kidgell DJ, Warmington SA. Unilateral bicep curl hemodynamics: Low-pressure continuous vs high-pressure intermittent blood flow restriction. *Scand J Med Sci Sport*. 2015;25(6):770-777. doi:10.1111/sms.12297.
7. Fahs CA, Loenneke JP, Rossow LM, Thiebaud RS, Bemben MG. Methodological considerations for blood flow restricted resistance exercise. *J Trainology*. 2012;1:14-22. doi:10.17338/trainology.1.1_14.
8. Sharma J, Salhotra R. Tourniquets in orthopedic surgery. *Indian J Orthop*. 2012;46(4):377. doi:10.4103/0019-5413.98824.
9. Rorabeck CH, Kennedy JC. Tourniquet-induced nerve ischemia complicating knee ligament surgery. *Am J Sports Med*. 1980;8(2):98-102. doi:10.1177/036354658000800207.
10. Patterson SD, Brandner CR. The role of blood flow restriction training for applied practitioners: A questionnaire-based survey. *J Sports Sci*. 2017;36(2):123-130. doi:10.1080/02640414.2017.1284341.
11. World Medical Association. World Medical Association declaration of Helsinki: Ethical principles for medical research involving human subjects. *J Am Med Assoc*. 2013;310(20):2191-2194. doi:10.1001/jama.2013.281053.
12. Loenneke JP, Thiebaud RS, Fahs CA, Rossow LM, Abe T, Bemben MG. Blood flow restriction does not result in prolonged decrements in torque. *Eur J Appl Physiol*. 2013;113(4):923-931. doi:10.1007/s00421-012-2502-x.
13. McEwen JA, Jeyasurya J, Owens J. How can personalised tourniquet systems accelerate rehabilitation of wounded warriors, professional athletes and orthopaedic patients? In: *39th of The Canadian Medical and Biological Engineering Conference*. ; 2016.
14. Roth KE, Mandryka B, Maier GS, et al. In-vivo analysis of epicutaneous pressure distribution beneath a femoral tourniquet - An observational study. *BMC Musculoskelet Disord*. 2015;16(1):1. doi:10.1186/s12891-015-0454-0.
15. Graham B, Breault MJ, McEwen JA, McGraw RW. Perineural pressures under the pneumatic tourniquet in the upper extremity. *J Hand Surg Am*. 1992;17(3):262-266. doi:10.1016/0266-7681(92)90111-E.
16. Loenneke JP, Fahs CA, Rossow LM, et al. Effects of cuff width on arterial occlusion: Implications for blood flow restricted exercise. *Eur J Appl Physiol*. 2012;112(8):2903-2912. doi:10.1007/s00421-011-2266-8.
17. Jessee MB, Buckner SL, Dankel SJ, Counts BR, Abe T, Loenneke JP. The Influence of Cuff Width, Sex, and Race on Arterial Occlusion: Implications for Blood Flow Restriction Research. *Sport Med*. 2016;46(6):913-921. doi:10.1007/s40279-016-0473-5.
18. Shimizu R, Hotta K, Yamamoto S, et al. Low-intensity resistance training with blood flow restriction improves vascular endothelial function and peripheral blood circulation in healthy elderly people. *Eur J Appl Physiol*. 2016;116(4):749-757. doi:10.1007/s00421-016-3328-8.
19. Borg G. *Borg's Perceived Exertion and Pain Scales*. Human Kinetics; 1998. doi:10.1097/00005768-199809000-00018.

20. Jessee MB, Dankel SJ, Buckner SL, Mouser JG, Mattocks KT, Loenneke JP. The Cardiovascular and Perceptual Response to Very Low Load Blood Flow Restricted Exercise. *Int J Sports Med*. 2017;38(8):597-603. doi:10.1055/s-0043-109555.
21. Dankel S, Buckner S, Counts B, et al. The acute muscular response to two distinct blood flow restriction protocols. *Physiol Int*. 2017;104(1):64-76. doi:10.1556/2060.104.2017.1.1.
22. Bland MJ, Altman DG. Statistical Methods for Assessing Agreement Between Two Methods of Clinical Measurement. *Lancet*. 1986;327(8476):307-310. doi:10.1016/S0140-6736(86)90837-8.
23. McEwen JA. Complications of and improvements in pneumatic tourniquets used in surgery. *Med Instrum*. 1981;15(4):253-257.
24. McLaren AC, Rorabeck CH. The pressure distribution under tourniquets. *J Bone Joint Surg Am*. 1985;67(3):433-438.
25. Martín-Hernández J, Ruiz-Aguado J, Herrero AJ, et al. Adaptation of Perceptual Responses to Low-Load Blood Flow Restriction Training. *J Strength Cond Res*. 2017;31(3):765-772. doi:10.1519/JSC.0000000000001478.
26. Mattocks KT, Jessee MB, Counts BR, et al. The effects of upper body exercise across different levels of blood flow restriction on arterial occlusion pressure and perceptual responses. *Physiol Behav*. 2017;171:181-186. doi:10.1016/j.physbeh.2017.01.015.
27. Yasuda T, Abe T, Brechue WF, et al. Venous blood gas and metabolite response to low-intensity muscle contractions with external limb compression. *Metabolism*. 2010;59(10):1510-1519. doi:10.1016/j.metabol.2010.01.016.
28. Takarada Y, Nakamura Y, Aruga S, et al. Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion restriction Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. *J Appl Physiol*. 2000;88:61-65.
29. Estebe JP, Le Naoures A, Chemaly L, Ecoffey C. Tourniquet pain in a volunteer study: Effect of changes in cuff width and pressure. *Anaesthesia*. 2000;55(1):21-26. doi:10.1046/j.1365-2044.2000.01128.x.
30. McEwen JA, Inkpen K. Safety preventing skin injuries. *Surg Technol*. 2002;34(August 2002):7-15.
31. Loenneke J, Thiebaud RS, Fahs CA, Rossow LM, Abe T, Bemben MG. Blood flow restriction: Effects of cuff type on fatigue and perceptual responses to resistance exercise. *Acta Physiol Hung*. 2014;101(2):158-166. doi:10.1556/APhysiol.101.2014.2.4.
32. Loenneke JP, Thiebaud RS, Fahs CA, Rossow LM, Abe T, Bemben MG. Effect of cuff type on arterial occlusion. *Clin Physiol Funct Imaging*. 2013;33(4):325-327. doi:10.1111/cpf.12035.
33. Lins-Filho ODL, Robertson RJ, Farah BQ, Rodrigues SL., Cyrino ES, Ritti-Dias RM. Effects of Exercise Intensity on Rating of Perceived Exertion During a Multiple-Set Resistance Exercise Session. *J Strength Cond Res*. 2012;26(2):466-472. doi:10.1519/JSC.0b013e31822602fa.
34. Hollander DB, Reeves G V., Clavier JD, Francois MR, Thomas C, Kraemer RR. Partial occlusion during resistance exercise alters effort sense and pain. *J Strength Cond Res*. 2010;24(1):235-243. doi:10.1519/JSC.0b013e3181c7badf.
35. Rossow LM, Fahs CA, Loenneke JP, et al. Cardiovascular and perceptual responses to blood-flow-restricted resistance exercise with differing restrictive cuffs. *Clin Physiol Funct Imaging*. 2012;32(5):331-337. doi:10.1111/j.1475-097X.2012.01131.x.
36. Mouser JG, Dankel SJ, Jessee MB, et al. A tale of three cuffs: the hemodynamics of blood flow restriction. *Eur J Appl Physiol*. 2017;117(7):1493-1499. doi:10.1007/s00421-017-3644-7.
37. Brandner CR, Warmington SA, Kidgell DJ. Corticomotor Excitability is Increased Following an Acute Bout of Blood Flow Restriction Resistance Exercise. *Front Hum Neurosci*. 2015;9:1-18. doi:10.3389/fnhum.2015.00652.
38. Adams J, Cline MJ, Hubbard M, McCullough T, Hartman J. A new paradigm for post-cardiac event resistance exercise guidelines. *Am J Cardiol*. 2006;97(2):281-286. doi:10.1016/j.amjcard.2005.08.035.

39. Cezar MA, De Sá CA, Corralo V da S, Copatti SL, Santos GAG dos, Grigoletto ME da S. Effects of exercise training with blood flow restriction on blood pressure in medicated hypertensive patients. *Mot rev educ fís*. 2016;22(2):9-17. doi:10.1590/S1980-6574201600020002.
40. Madarame H, Kurano M, Fukumura K, Fukuda T, Nakajima T. Haemostatic and inflammatory responses to blood flow-restricted exercise in patients with ischaemic heart disease: A pilot study. *Clin Physiol Funct Imaging*. 2013;33(1):11-17. doi:10.1111/j.1475-097X.2012.01158.x.

Table 1. BFR pressures, load, leg circumference and sensor distance across the three different BFR cuffs (Mean ± SD)

	RI	PT	HS
BFR pressures (mmHg)			
LOP	163.33 ± 17.06	176.56 ± 19.22*	215.56 ± 20.36#†
Exercise trial			
80% LOP (Set pressure)	130 ± 14	141 ± 15	172 ± 16
80% LOP (Interface pressure)	+10 ± 8[b]	-2 ± 7	+48 ± 36[b]
Rest trial			
80% LOP (Set pressure)	130 ± 14	141 ± 15	172 ± 16
80% LOP (Interface pressure)	-5 ± 5[a]	-9 ± 4[a]	-37 ± 13[a]
40% LOP (Set pressure)	65 ± 7	71 ± 8	85 ± 9
40% LOP (Interface pressure)	-5 ± 5[a]	-8 ± 4[a]	-20 ± 10[a]
Load (kg)			
1RM		178 ± 57	
30% 1RM		53 ± 17	
Leg circumference (cm)			
Proximal	61 ± 5	64 ± 4	61 ± 4
Distal	52 ± 5	55 ± 5	57 ± 5
Midline	58 ± 5	59 ± 5	59 ± 5
Distance between sensors (cm)	14.7 ± 1.0	14.7 ± 1.0	14.9 ± 1.2

* = significantly higher than RI system ($p<0.05$); # = significantly higher than RI system ($p<0.01$); † = significantly higher PT system ($p<0.01$); a = significantly different to set pressure ($p<0.05$); b = significantly different to set pressure ($p<0.01$).

Table 2: Pain, RPE and MAP across the three different BFR systems (Mean ± SD)

	RI	PT	HS
Pain (au)			
Set 1	2.4 ± 1.4	2.0 ± 1.4	3.0 ± 1.6
Set 2	4.1 ± 2.0*	3.5 ± 1.6*	4.6 ± 1.8*†
Set 3	6.8 ± 2.8*†	4.8 ± 1.8*	7.0 ± 2.5*†
Set 4	7.9 ± 2.3*†	5.7 ± 2.0*	8.3 ± 2.3*†
RPE (au)			
Set 1	11 ± 2	11 ± 2	12 ± 2
Set 2	14 ± 2*	13 ± 0*	14 ± 1*†
Set 3	15 ± 2*	14 ± 2*	16 ± 2*†
Set 4	17 ± 2*†	15 ± 2*	17 ± 2*†
MAP (mmHg)			
Pre-exercise	102 ± 9	100 ± 9	104 ± 7
1-min post	116 ± 10^{a†}	105 ± 9	116 ± 9^{a†}
5-min post	108 ± 5†	99 ± 11^{a}	110 ± 9^{a†}

* = significantly higher than previous set ($p<0.05$); † = significantly higher than PT cuff trial ($p<0.01$); a = significantly different to pre-exercise ($p<0.05$).

Figure 1. Set up of BFR cuff and pressure sensors for the rest and exercise trials

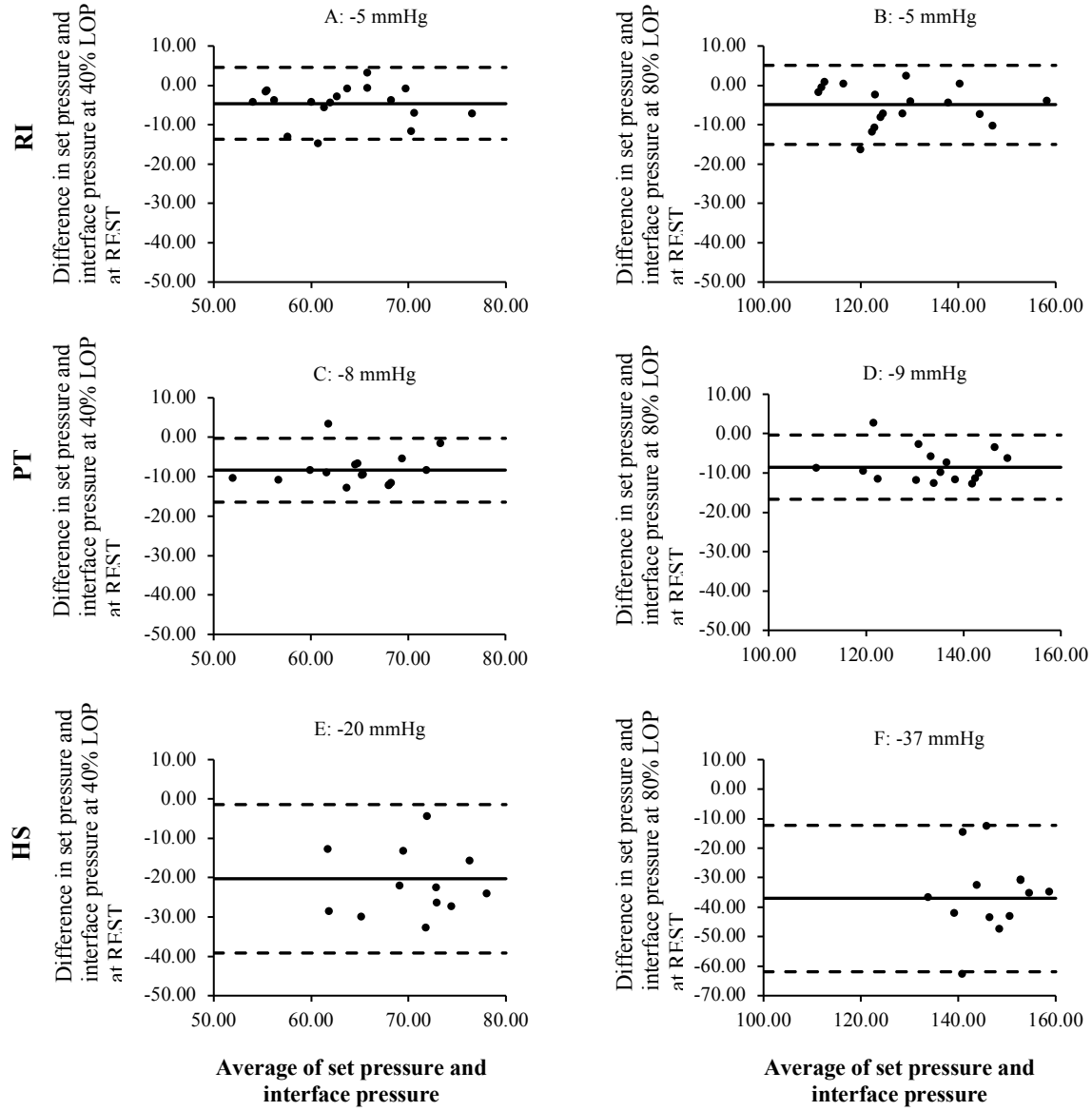

Figure 2. Bland and Altman plot of the mean difference between set pressure and interface pressure (mmHg) with 95% LOAs during the rest trial (RI system at 40% and 80% LOP = A and B, respectively; PT system at 40% and 80% LOP = C and D, respectively; HS system at 40% and 80% LOP = E and F, respectively).

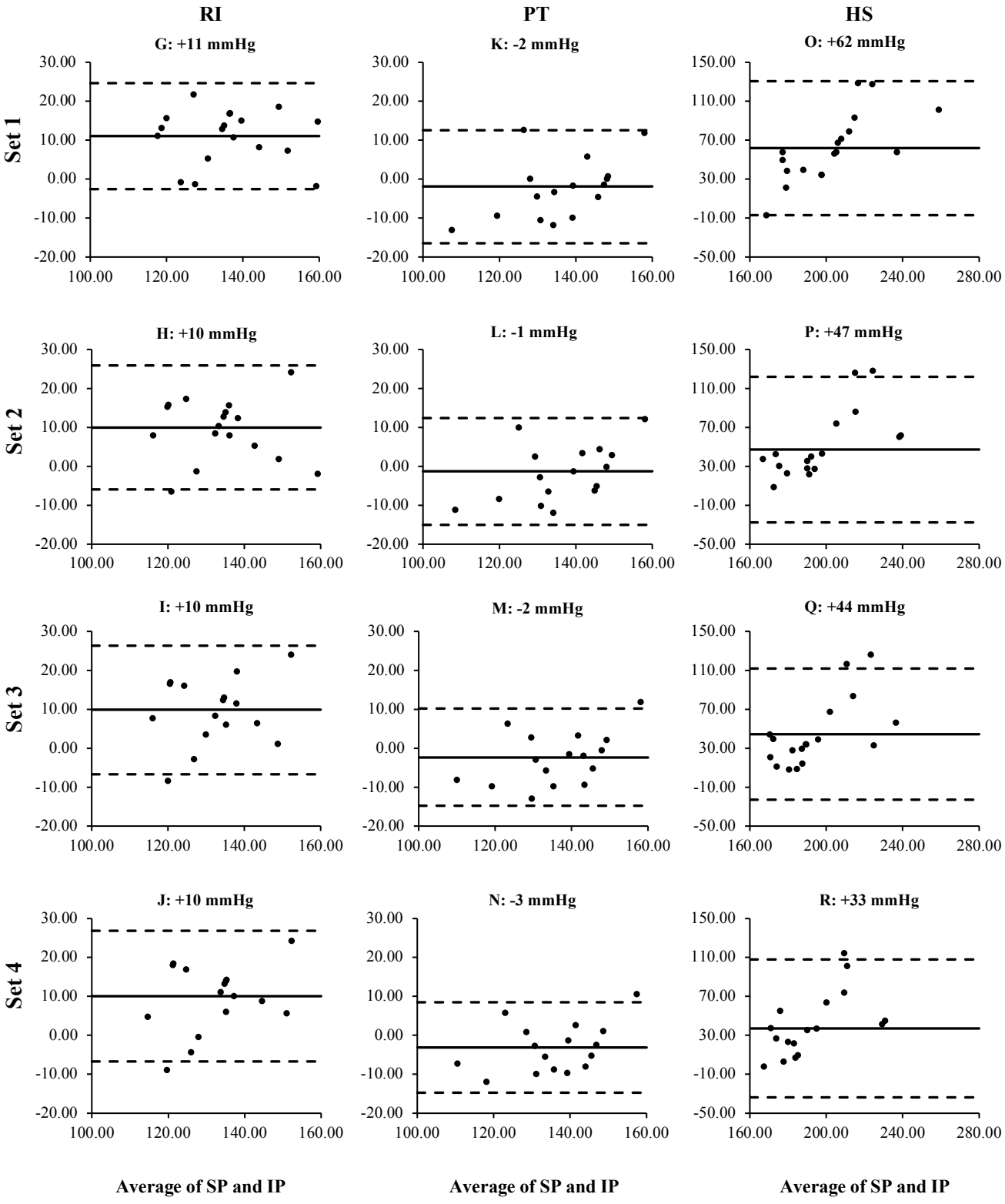

Figure 3. Bland and Altman plots of the mean difference between set pressure and interface pressure (mmHg) with 95% LOAs across 4 sets during the exercise trial for the RI system (G, H, I and J), PT system (K, L, M and N), and HS system (O, P, Q and R), respectively.